PATENT

SEQUENCE LISTING

<110>	Donna T. Ward
	William Gaarde
	Brett P. Monia
	Jacqueline Wyatt

- <120> ANTISENSE MODULATION OF MEKK4 EXPRESSION
- <130> RTS-0169
- <160> 89
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- <211> 20
- <212> DNA
- <213> Artificial Sequence
- <223> Antisense Oligonucleotide
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- <210> 2
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145

RTS-0169 -2-	
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10 15	
1 5	
tot dec dec age aca det ega dag atg aaa ege atg tea ade aaa dat	96
Ser Pro Pro Ser Thr Pro Arg Gln Met Lys Arg Met Ser Thr Lys His	
20 25 30	
	144
cag agg aat aat gtg ggg agg cca gcc agt cgg tct aat ttg aaa gaa	144
Gln Arg Asn Asn Val Gly Arg Pro Ala Ser Arg Ser Asn Leu Lys Glu	
35 40 45	
aaa atg aat gca cca aat cag cct cca cat aaa gac act gga aaa aca	192
Lys Met Asn Ala Pro Asn Gln Pro Pro His Lys Asp Thr Gly Lys Thr	
50 55 60	
30	
gtg gag aat gtg gaa gaa tac agc tat aag cag gag aaa aag atc cga	240
Val Glu Asn Val Glu Glu Tyr Ser Tyr Lys Gln Glu Lys Lys 11e Arg	
65 70 75 80	
	288
gca gct ctt aga aca aca gag cgt gat cat aaa aaa aat gta cag tgc	200
Ala Ala Leu Arg Thr Thr Glu Arg Asp His Lys Lys Asn Val Gln Cys 90 95	
85 90	
tca ttc atg tta gac tca gtg ggt gga tct ttg cca aaa aaa tca att	336
Ser Phe Met Leu Asp Ser Val Gly Gly Ser Leu Pro Lys Lys Ser Ile	
100 105 110	
cca gat gtg gat ctc aat aag cct tac ctc agc ctt ggc tgt agc aat	384
Pro Asp Val Asp Leu Asn Lys Pro Tyr Leu Ser Leu Gly Cys Ser Asn	
115 120 125	
	432
get aag ett eea gta tet gtg eee atg eet ata gee aga eet gea ege	432
Ala Lys Leu Pro Val Ser Val Pro Met Pro Ile Ala Arg Pro Ala Arg	
130 135 140	
cag act tot agg act gac tgt cca gca gat cgt tta aag ttt ttt gaa	480
Gln Thr Ser Arg Thr Asp Cys Pro Ala Asp Arg Leu Lys Phe Phe Glu	
145 150 155 160	

-2-

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act tta cga ctt ttg cta aag ctt acc tca gtc tca aag aaa aaa gac Thr Leu Arg Leu Leu Leu Lys Leu Thr Ser Val Ser Lys Lys Asp agg gag caa aga gga caa gaa aat acg tct ggt ttc tgg ctt aac cga Arg Glu Gln Arg Gly Gln Glu Asn Thr Ser Gly Phe Trp Leu Asn Arg tct aac gaa ctg atc tgg tta gag cta caa gcc tgg cat gca gga cgg Ser Asn Glu Leu Ile Trp Leu Glu Leu Gln Ala Trp His Ala Gly Arg aca att aac gac cag gac ttc ttt tta tat aca gcc cgt caa gcc atc Thr Ile Asn Asp Gln Asp Phe Phe Leu Tyr Thr Ala Arg Gln Ala Ile cca gat att att aat gaa atc ctt act ttc aaa gtc gac tat ggg agc Pro Asp Ile Ile Asn Glu Ile Leu Thr Phe Lys Val Asp Tyr Gly Ser ttc gcc ttt gtt aga gat aga gct ggt ttt aat ggt act tca gta gaa Phe Ala Phe Val Arg Asp Arg Ala Gly Phe Asn Gly Thr Ser Val Glu ggg cag tgc aaa gcc act cct gga aca aag att gta ggt tac tca aca Gly Gln Cys Lys Ala Thr Pro Gly Thr Lys Ile Val Gly Tyr Ser Thr cat cat gag cat ctc caa cgc cag agg gtc tca ttt gag cag gta aaa His His Glu His Leu Gln Arg Gln Arg Val Ser Phe Glu Gln Val Lys cgg ata atg gag ctg cta gag tac ata gaa gca ctt tat cca tca ttg Arg Ile Met Glu Leu Leu Glu Tyr Ile Glu Ala Leu Tyr Pro Ser Leu cag gct ctt cag aag gac tat gaa aaa tat gct gca aaa gac ttc cag Gln Ala Leu Gln Lys Asp Tyr Glu Lys Tyr Ala Ala Lys Asp Phe Gln gac agg gtg cag gca ctc tgt ttg tgg tta aac atc aca aaa gac tta

Asp Arg Val Gln Ala Leu Cys Leu Trp Leu Asn Ile Thr Lys Asp Leu

-3-

-4-RTS-0169 aat cag aaa tta agg att atg ggc act gtt ttg ggc atc aag aat tta Asn Gln Lys Leu Arg Ile Met Gly Thr Val Leu Gly Ile Lys Asn Leu tca gac att ggc tgg cca gtg ttt gaa atc cct tcc cct cga cca tcc Ser Asp Ile Gly Trp Pro Val Phe Glu Ile Pro Ser Pro Arg Pro Ser aaa ggt aat gag ccg gag tat gag ggt gat gac aca gaa gga gaa tta Lys Gly Asn Glu Pro Glu Tyr Glu Gly Asp Asp Thr Glu Gly Glu Leu aag gag ttg gaa agt agt acg gat gag agt gaa gaa gaa caa atc tct Lys Glu Leu Glu Ser Ser Thr Asp Glu Ser Glu Glu Glu Gln Ile Ser gat cct agg gta ccg gaa atc aga cag ccc ata gat aac agc ttc gac Asp Pro Arg Val Pro Glu Ile Arg Gln Pro Ile Asp Asn Ser Phe Asp atc cag tcg cgg gac tgc ata tcc aag aag ctt gag agg ctc gaa tct Ile Gln Ser Arg Asp Cys Ile Ser Lys Leu Glu Arg Leu Glu Ser gag gat gat tot ott ggo tgg gga gca cca gac tgg agc aca gaa gca Glu Asp Asp Ser Leu Gly Trp Gly Ala Pro Asp Trp Ser Thr Glu Ala ggc ttt agt aga cat tgt ctg act tct att tat aga cca ttt gta gac Gly Phe Ser Arg His Cys Leu Thr Ser Ile Tyr Arg Pro Phe Val Asp aaa gca ctg aag cag atg ggg tta aga aag tta att tta aga ctt cac Lys Ala Leu Lys Gln Met Gly Leu Arg Lys Leu Ile Leu Arg Leu His aag cta atg gat ggt tcc ttg caa agg gca cgt ata gca ttg gta aag Lys Leu Met Asp Gly Ser Leu Gln Arg Ala Arg Ile Ala Leu Val Lys aac gat cgt cca gtg gag ttt tct gaa ttt cca gat ccc atg tgg ggt Asn Asp Arg Pro Val Glu Phe Ser Glu Phe Pro Asp Pro Met Trp Gly

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tgc Cys	agt Ser 530	gct Ala	gtg Val	tcg Ser	tgg Trp	gag Glu 535	gag Glu	ctg Leu	aag Lys	gcc Ala	atg Met 540	gat Asp	tta Leu	cct Pro	tca Ser	1632
ttc Phe 545	gaa Glu	cct Pro	gcc Ala	ttc Phe	cta Leu 550	gtt Val	ctc Leu	tgc Cys	cga Arg	gtc Val 555	ctt Leu	ctg Leu	aat Asn	gtc Val	ata Ile 560	1680
cat His	gag Glu	tgt Cys	ctg Leu	aag Lys 565	tta Leu	aga Arg	ttg Leu	gag Glu	cag Gln 570	aga Arg	cct Pro	gct Ala	gga Gly	gaa Glu 575	cca Pro	1728
tct Ser	ctc Leu	ttg Leu	agt Ser 580	att Ile	aag Lys	cag Gln	ctg Leu	gtg Val 585	aga Arg	gag Glu	tgt Cys	aag Lys	gag Glu 590	Val	ctg Leu	1776
a ag Lys	ggc Gly	ggo Gly 595	ctg Leu	ctg Leu	atg Met	aag Lys	cag Gln 600	Tyr	tac Tyr	cag Gln	ttc Phe	atg Met	Leu	cag Gln	gag Glu	1824
gtt Va]	ctg Lev	ı Glı	g gac ı Asp	ttg Leu	gag Glu	aag Lys 615	Pro	gac Asp	tgc Cys	aac Asr	att 11e 620	Asp	gct Ala	ttt a Phe	gaa Glu	1872
gaq Glu	ı Asp	cta Le	a cat u His	aaa Lys	atg Met	Leu	at <u>c</u> Met	g gtg : Val	, tat L Tyr	ttt Phe	e Asp	tac y Tyi	c ato	g aga	a agc g Ser 640	1920
tg:	g ato	c ca e Gl	a atq n Met	g cta t Lev 649	ı Glr	g caa n Glr	ı tta	a cct	caa Glr 650	n Ala	a tog a Se:	g cat	t ag	t tta r Le: 65!	a aaa 1 Lys 5	1968
aa As	t ct	g tt u Le	a ga u Gl [.] 66	u Gl	a gaa u Gli	a tgg u Trj	g aa o As:	t tte n Ph	e Th	c aa r Ly	a ga s Gl	a at u Il	a ac e Th 67	r Hi	t tac s Tyr	2016
at Il	a cg e Ar	g gg g Gl 67	y Gl	a ga y Gl	a gca	a cag a Gli	g gc n Al 68	a Gl	g aa y Ly	g ct s Le	t tt u Ph	c tg e Cy 68	s As	c at p Il	t gca e Ala	2064

-6-RTS-0169 gga atg ctg ctg aaa tct aca gga agt ttt tta gaa ttt ggc tta cag 2112 Gly Met Leu Leu Lys Ser Thr Gly Ser Phe Leu Glu Phe Gly Leu Gln 700 695 690 gag agc tgt gct gaa ttt tgg act agt gcg gat gac agc agt gct tcc 2160 Glu Ser Cys Ala Glu Phe Trp Thr Ser Ala Asp Asp Ser Ser Ala Ser 710 705 gac gaa atc agg agg tct gtt ata gag atc agt cga gcc ctg aag gag 2208 Asp Glu Ile Arg Arg Ser Val Ile Glu Ile Ser Arg Ala Leu Lys Glu 735 730 725 ctc ttc cat gaa gcc aga gaa agg gct tcc aaa gca ctt gga ttt gct 2256 Leu Phe His Glu Ala Arg Glu Arg Ala Ser Lys Ala Leu Gly Phe Ala 745 740 aaa atg ttg aga aag gac ctg gaa ata gca gca gaa ttc agg ctt tca 2304 Lys Met Leu Arg Lys Asp Leu Glu Ile Ala Glu Phe Arg Leu Ser 765 760 755 gcc cca gtt aga gac ctc ctg gat gtt ctg aaa tca aaa cag tat gtc 2352 Ala Pro Val Arg Asp Leu Leu Asp Val Leu Lys Ser Lys Gln Tyr Val 780 775 770 aag gtg caa att cct ggg tta gaa aac ttg caa atg ttt gtt cca gac 2400 Lys Val Gln Ile Pro Gly Leu Glu Asn Leu Gln Met Phe Val Pro Asp 800 795 790 785 act ctt gct gag gag aag agt att att ttg cag tta ctc aat gca gct 2448 Thr Leu Ala Glu Glu Lys Ser Ile Ile Leu Gln Leu Leu Asn Ala Ala 815 810 805 gca gga aag gac tgt tca aaa gat tca gat gac gta ctc atc gat gcc 2496 Ala Gly Lys Asp Cys Ser Lys Asp Ser Asp Asp Val Leu Ile Asp Ala 830 825 820 tat ctg ctt ctg acc aag cac ggt gat cga gcc cgt gat tca gag gac 2544 Tyr Leu Leu Leu Thr Lys His Gly Asp Arg Ala Arg Asp Ser Glu Asp 845 840 835 age tgg ggc acc tgg gag gca cag cct gtc aaa gtc gtg cct cag gtg 2592 Ser Trp Gly Thr Trp Glu Ala Gln Pro Val Lys Val Val Pro Gln Val 860 855 850

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gag a	act	qtt	gac	acc	ctg	aga	agc	atg	cag	gtg	gat	aat	ctt	tta	cta	2640
Glu :	Гhr	Val	Asp	Thr	Leu	Arg	Ser	Met	Gln	Val	Asp	Asn	Leu	Leu	Leu	
865			_		870					875					880	
gtt	gtc	atg	cag	tct	gcg	cat	ctc	aca	att	cag	aga	aaa	gct	ttc	cag	2688
Val	Val	Met	Gln	Ser	Ala	His	Leu	Thr	Ile	Gln	Arg	Lys	Ala	Phe	Gln	
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																0726
cag	tcc	att	gag	gga	ctt	atg	act	ctg	tgc	cag	gag	cag	aca	tcc	agt	2736
Gln	Ser	Ile	Glu	Gly	Leu	Met	Thr	Leu	Cys	Gln	Glu	Gln		Ser	ser	
			900					905					910			
													~a+	~~~	++-	2784
cag	ccg	gtc	atc	gcc	aaa	gct	ttg	cag	cag	ctg	aag	aac	yar	gca	Leu	2,01
Gln	Pro	Val	Ile	Ala	Lys	Ala		GIn	GIn	ьeu	ьуѕ	925	Asp	Ala	пец	
		915					920					925				
					- 4			~~~	a++	aaa	. כמכ	ata	gac	cac	atq	2832
gag	cta	tgo	aac	agg	ata	age	Aan	ycc 71a	Tle	Δan	Δro	val	Asp	cac His	Met	
Glu			Asn	arg	TTE	935	ASII	AIG	110	ADE	940		F			
	930					933										
-	242	tas		. +++	gat	act	gag	att	gat	qaa	tct	gaa	tct	gtc	acc	2880
Dho	Thr		r Gli	. Dhe	Asp	Ala	Glu	Val	Asp	Glu	ı Ser	Glu	Ser	Val	Thr	
945	1111	261	. 010	1 1110	950				-	955					960	
945					,,,,,											
tta	caa	cac	r tac	tac	c cqa	qaa	gca	atg	att	cag	g gg	g tac	aat	ttt	gga	2928
Leu	Glr	ı Glı	ı Tyı	r Tyr	Arc	Glu	. Ala	Met	Ile	Glı	n Gly	у Туг	Asr	ı Ph∈	Gly	
204				965					970					975		
ttt	gag	g ta	t cat	t aaa	a gaa	gtt	gtt	. cgt	ttg	g at	g tc	t ggg	g gag	g ttt	aga	2976
Phe	Gli	1 Ту:	r His	в Гу	s Glu	ı Val	l Val	l Arc	j Lei	ı Me	t Se	r Gly	/ Glu	ı Phe	e Arg	
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cag	aa	g at	a gg	a ga	c aaa	a ta	ata	a ago	tt!	t gc	c cg	g aaq	g tg	g ato	g aat	3024
Gln	Ьу	s Il	e Gl	y As	р Ьу	з Ту	r Ile	e Sei	c Ph	e Al	a Ar			p Met	t Asn	
		99	5				10	00				10	05			
															~ +~~	3072
tat	gt	c ct	g ac	t aa	a tg	t ga	g ag	t gg!	t ag	a gg	t ac	a ag	a cc	c ag	g tgg	3072
Tyr	· Va	l Le	u Th	r Ly	в Су			r Gly	y Ar	g GI			g Pr	O AL	g Trp	
	10	10				10	15				10	20				
									. ~-	.	+ ~~		t ac	c tt	t att	3120
gcg	g ac	t ca	a gg	a tt	t ga	t tt - 51-	CC	a ca	a yc	а аL э т1	u ya ای م	11 Pr	O Al	a Ph	t att e Ile	•
		r Gl	n Gl	y Ph			e re	u GI	TI WI		35				1040)
102	25				10	30										

t a 2	aat	tta	cca	gaa	gat	gac	ttc	ttg	aqt	tta	caa	gcc	ttg	atg	aat	3168
Ser	Δla	Leu	Pro	Glu	Asp	Asp	Phe	Leu	Ser	Leu	Gln	Ala	Leu	Met	Asn	
501	AIG			1045		-			1050					1055		
qaa	tgc	att	ggc	cat	gtc	ata	gga	aaa	cca	cac	agt	cct	gtt	aca	ggt	3216
Glu	Cys	Ile	Gly	His	Val	Ile	Gly	Lys	Pro	His	Ser	Pro	Val	Thr	Gly	
			1060)				1065	5				1070)		
																2064
ttg	tac	ctt	gcc	att	cat	cgg	aac	agc	ccc	cgt	cct	atg	aag -	gta	cct	3264
Leu	Tyr	Leu	Ala	Ile	His	Arg		Ser	Pro	Arg	Pro			vaı	PIO	
		107	5				108	0				108	5			
										ata	a++	atc	ccc	act	cca	3312
cga	tgc	cat	agt	gac	cct	CCT	aac	cca	Uic	LAU	Tle	Tle	Pro	Thr	Pro	
Arg			Ser	Asp	Pro	109		Pro	пів	пеп	110		110	1111	110	
	109	١.	12			109					110	•				
		/ ++a	377	äät	Écc	a cicl	// att	cct	gaa	aat	gat	cga	ttg	gct	tcc	3360
gag	gga	Dhe	Arg	Glv	Ser	Ser	Val	Pro	Glu	Asn	Asp	Arg	Leu	Ala	Ser	
110		PIIC	ALG	Gry	111					111					1120	
110	5					_										
ata	act	act	gaa	ttg	cag	ttt	agg	tcc	ctg	agt	cgt	cac	tca	agc	ccc	3408
Ile	Ala	Ala	. Glu	Leu	Gln	Phe	Arg	Ser	Leu	Ser	Arg	, His	Ser	Ser	Pro	
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acg	gag	gag	g cga	gat	gaa	сса	gca	ı tat	cca	aga	ı gga	a gat	tca	agt	ggg	3456
Thr	Glu	ı Glı	ı Arç	Asp	Glu	Pro	Ala	a Tyr	Pro	Arg	g Gl	/ Asp			Gly	
			114	: 0				114	.5				115	50		
															- 222	3504
tco	aca	a aga	a aga	a agt	t tgg	gaa	ctt	cgg	g aca	a cta	aato	ago	caç	g agu	aaa Lyg	2204
Sei	Thi			g Sei	r Trp	GI1				с ьег	1 TT6	110		1 361	. Lys	
		11	55				T T 6	50				11,	,,			
					- c+	. ~~		~ ats	a da:	a act	t ato	c ca	g aad	g tca	a gtc	3552
ga	c act	t gc	ב ככי	ada	a CL	1 99°	, Dr	n Tle	a gad	ı Ala	a Il	e Gli	n Ly:	s Sei	r Val	
AS]	11.		a 5e.	г пу	ь пс	11'					11		-			
	11	70					, 0									
ca	a tt	a tt	t da	а ста	a aa	g aq	g ta	c cga	a ga	a at	g ag	g ag	a aa	g aa	t atc	3600
Δr	a Le	u Ph	e Gl	u Gl	u Ly	s Ar	- g Ту	r Ar	g Gl	u Me	t Ar	g Ar	g Ly	s As	n Ile	
11					11		- -			11					1200	
at	t gg	t ca	a gt	t tg	t ga	t ac	g cc	t aa	g tc	c ta	t ga	t aa	t gt	t at	g cac	3648
11	e Gl	y Gl	n Va	l Cy	s As	p Th	r Pr	o Ly	s Se	r Ty	r As	p As	n Va	1 Me	t His	
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Val	Gly	Leu	agg Arg 1220	Lys	Val	Thr	Phe	Lys 1225	Trp	Gln	Arg	Gly	Asn 1230	Lys	Ile	3696
gga Gly	gaa Glu	ggc Gly 123!	cag Gln	tat Tyr	GJA aaa	aag Lys	gtg Val 1240	Tyr	acc Thr	tgc Cys	atc Ile	agc Ser 1245	Val	gac Asp	acc Thr	3744
Gly 333	gag Glu 125	Leu	atg Met	gcc Ala	atg Met	aaa Lys 125	Glu	att Ile	cga Arg	ttt Phe	caa Gln 126	Pro	aat Asn	gac Asp	cat His	3792
aag Lys 126	Thr	atc Ile	aag Lys	gaa Glu	act Thr 127	Ala	gac Asp	gaa Glu	ttg Leu	aaa Lys 127	Ile	ttc Phe	gaa Glu	ggc Gly	atc Ile 1280	3840
aaa Lys	cac His	ccc Pro	aat Asn	ctg Leu 128	Val	cgg Arg	tat Tyr	ttt Phe	ggt Gly 129	Val	gag Glu	ctc Leu	cat His	aga Arg 129	Glu	3888
gaa Glu	atg Met	tac Tyr	atc Ile 130	Phe	atg Met	gag Glu	tac Tyr	tgc Cys 130	Asp	gag Glu	ggg Gly	act Thr	tta Leu 131	Glu	gag Glu	3936
gtg Val	tca Ser	agg Arg	g Leu	gga Gly	ctt Leu	cag Gln	gaa Glu 132	His	gtg Val	att Ile	agg Arg	g ctg Leu 132	Tyr	tca Ser	aag Lys	3984
ca <u>c</u> Glr	ato 133	e Thi	c att	gcg Ala	ato Ile	aac Asr 133	ı Val	cto L Lei	c cat ı His	gag Glu	cat His	₃ Glչ	ata / Ile	gto Val	cac His	4032
cgt Arg	g Asj	c at	t aaa e Lys	ggt Gl	gco Ala	a Ası	ato	c tto	c ctt	acc Thi	r Se	a tct r Sei	gga Gly	a tta / Lei	a atc 1 Ile 1360	4080
aaa Lys	a cto s Le	g gg u Gl	a gat y Ası	ttt Phe	e Gly	a tgi y Cy:	t tc	a gta	a aaq l Ly: 13'	s Le	c aa u Ly	a aa s As:	c aat n Ası	gco n Ala 13'	c cag a Gln 75	4128
ac Th	c at r Me	g cc t Pr	t gg o Gly	y Gl	a gte	g aa l As:	c ag n Se	c ac r Th 13	r Le	g gg u Gl	g ac y Th	a gc r Al	a gca a Ala 13	а Ту	c atg r Met	4176

RTS-0169 -10-	ATENT
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gcc gac atc tgg agt ctg ggg tgt gtt gtc ata gag atg gtg act ggc Ala Asp Ile Trp Ser Leu Gly Cys Val Val Ile Glu Met Val Thr Gly 1410 1415 1420	4272
aag agg cct tgg cat gag tat gag cac aac ttt caa att atg tat aaaLys Arg Pro Trp His Glu Tyr Glu His Asn Phe Gln Ile Met Tyr Lys14251430	4320
gtg ggg atg gga cat aag cca cca atc cct gaa aga tta agc cct gaa Val Gly Met Gly His Lys Pro Pro Ile Pro Glu Arg Leu Ser Pro Glu 1445 1450 1455	4368
gga aag gac ttc ctt tct cac tgc ctt gag agt gac cca aag atg aga Gly Lys Asp Phe Leu Ser His Cys Leu Glu Ser Asp Pro Lys Met Arg 1460 1465 1470	4416
tgg acc gcc agc cag ctc ctc gac cat tcg ttt gtc aag gtt tgc aca Trp Thr Ala Ser Gln Leu Leu Asp His Ser Phe Val Lys Val Cys Thr 1475 1480 1485	4464
gat gaa gaa tga agcctagtag aatatggact tggaaaattc tcttaatcac Asp Glu Glu XXX 1490	4516
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PATENT

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	172
ccatgcgggg ctccgtgcac gg atg aga gaa gcc gct gcc gcg ctg gtc cct	1/2
Met Arg Glu Ala Ala Ala Leu Val Pro 1 5 10	
1 5 10	
cct ccc gcc ttt gcc gtc acg cct gcc gcc atg gag gag ccg ccg	220
Pro Pro Ala Phe Ala Val Thr Pro Ala Ala Met Glu Glu Pro Pro	

RTS	-01	69						- 1	L3 -							PATENT
				15					20					25		
	_	_	_	_	cca Pro		_		_	_						268
_			_		ttg Leu											316
	_	_	_	_	cct Pro	_		-		_	-			_	_	364
					ctt Leu 80							_			_	412
_	_		_	_	tca Ser				_							460
	_	_			aat Asn	_		_		_		_			_	508
				_	act Thr								_	_		556
_		_	_		aaa Lys	_		_	_	_		_				604
_	_				aat Asn 160	-	_	_			-		-			652
			_		aaa Lys					_		_			_	700
			_		ggc Glv	_	_		_	_			_			748

RTS-0169 -14-PATENT 195 200 190 796 ccc atg cct ata gcc aga cct gca cgc cag act tct agg act gac tgt Pro Met Pro Ile Ala Arq Pro Ala Arg Gln Thr Ser Arg Thr Asp Cys 205 210 215 cca gca gat cgt tta aag ttt ttt gaa act tta cga ctt ttg cta aag 844 Pro Ala Asp Arg Leu Lys Phe Phe Glu Thr Leu Arg Leu Leu Lys 220 225 230 ctt acc tca gtc tca aag aaa aaa gac agg gag caa aga gga caa gaa 892 Leu Thr Ser Val Ser Lys Lys Lys Asp Arg Glu Gln Arg Gly Gln Glu 240 235 aat acg tot ggt tto tgg ott aac cga tot aac gaa otg ato tgg tta 940 Asn Thr Ser Gly Phe Trp Leu Asn Arg Ser Asn Glu Leu Ile Trp Leu 255 260 265 988 gag cta caa gcc tgg cat gca gga cgg aca att aac gac cag gac ttc Glu Leu Gln Ala Trp His Ala Gly Arg Thr Ile Asn Asp Gln Asp Phe 280 270 275 ttt tta tat aca gcc cgt caa gcc atc cca gat att att aat gaa atc 1036 Phe Leu Tyr Thr Ala Arg Gln Ala Ile Pro Asp Ile Ile Asn Glu Ile 285 290 ctt act ttc aaa gtc gac tat ggg agc ttc gcc ttt gtt aga gat aga 1084 Leu Thr Phe Lys Val Asp Tyr Gly Ser Phe Ala Phe Val Arg Asp Arg 300 305 gct ggt ttt aat ggt act tca gta gaa ggg cag tgc aaa gcc act cct 1132 Ala Gly Phe Asn Gly Thr Ser Val Glu Gly Gln Cys Lys Ala Thr Pro 315 320 325 330

cag agg gtc tca ttt gag cag gta aaa cgg ata atg gag ctg cta gag 1228
Gln Arg Val Ser Phe Glu Gln Val Lys Arg Ile Met Glu Leu Leu Glu
350 355 360
tac ata gaa gca ctt tat cca tca ttg cag gct ctt cag aag gac tat 1276

1180

gga aca aag att gta ggt tac tca aca cat cat gag cat ctc caa cgc

Gly Thr Lys Ile Val Gly Tyr Ser Thr His His Glu His Leu Gln Arg

Tyr Ile Glu Ala Leu Tyr Pro Ser Leu Gln Ala Leu Gln Lys Asp Tyr

RTS-0169	-15-		PATENT
365	370	375	
7. 7.		agg gtg cag gca ctc tgt Arg Val Gln Ala Leu Cys 390	1324
	<u> </u>	cag aaa tta agg att atg Gln Lys Leu Arg Ile Met 405 410	1372
	y Ile Lys Asn Leu Ser	gac att ggc tgg cca gtg Asp Ile Gly Trp Pro Val 425	1420
	<u> </u>	ggt aat gag ccg gag tat Gly Asn Glu Pro Glu Tyr 440	1468
		gag ttg gaa agt agt acg Glu Leu Glu Ser Ser Thr 455	1516
	_	cct agg gta ccg gaa atc Pro Arg Val Pro Glu Ile 470	1564
		cag tcg cgg gac tgc ata Gln Ser Arg Asp Cys Ile 485 490	1612
3 4 3	ı Arg Leu Glu Ser Glu	gat gat tot ott ggo tgg Asp Asp Ser Leu Gly Trp 505	1660
		ttt agt aga cat tgt ctg Phe Ser Arg His Cys Leu 520	1708
V V		gca ctg aag cag atg ggg Ala Leu Lys Gln Met Gly 535	1756
	-	cta atg gat ggt tcc ttg Leu Met Asp Gly Ser Leu	1804

RTS-0169	-16-	PATENT
540	545 550	
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-	at ccc atg tgg ggt tca gat tat gtg cag ttg sp Pro Met Trp Gly Ser Asp Tyr Val Gln Leu 580 585	
	ca tot gag gag aaa tgo agt got gtg tog tgg er Ser Glu Glu Lys Cys Ser Ala Val Ser Trp 595 600	
	tg gat tta cct tca ttc gaa cct gcc ttc cta et Asp Leu Pro Ser Phe Glu Pro Ala Phe Leu 610 615	7
	tt ctg aat gtc ata cat gag tgt ctg aag tta eu Leu Asn Val Ile His Glu Cys Leu Lys Leu 625 630	
	ct gct gga gaa cca tct ctc ttg agt att aag ro Ala Gly Glu Pro Ser Leu Leu Ser Ile Lys 640 645	
Leu Val Arg Glu Cy	gt aag gag gtc ctg aag ggc ggc ctg ctg atg ys Lys Glu Val Leu Lys Gly Gly Leu Leu Met 660 665	
	tc atg ctg cag gag gtt ctg gag gac ttg gag he Met Leu Gln Glu Val Leu Glu Asp Leu Glu 675 680	
	tt gac gct ttt gaa gag gat cta cat aaa atg le Asp Ala Phe Glu Glu Asp Leu His Lys Met 690 695	
	at tac atg aga agc tgg atc caa atg cta cag sp Tyr Met Arg Ser Trp Ile Gln Met Leu Gln 705 710	
_	cg cat agt tta aaa aat ctg tta gaa gaa gaa er His Ser Leu Lys Asn Leu Leu Glu Glu Glu	9.5

RTS-0169	-17-	PATENT
715	720 725 730	
_	ata act cat tac ata cgg gga gga gaa gca cag Ile Thr His Tyr Ile Arg Gly Gly Glu Ala Gln 740 745	2380
	tgt gac att gca gga atg ctg ctg aaa tct aca Cys Asp Ile Ala Gly Met Leu Leu Lys Ser Thr 755 760	2428
55 5	ttt ggc tta cag gag agc tgt gct gaa ttt tgg Phe Gly Leu Gln Glu Ser Cys Ala Glu Phe Trp 770 775	2476
5 5 5 5	agc agt gct tcc gac gaa atc atc agg tct gtt Ser Ser Ala Ser Asp Glu Ile Ile Arg Ser Val 785 790	2524
	gcc ctg aag gag ctc ttc cat gaa gcc aga gaa Ala Leu Lys Glu Leu Phe His Glu Ala Arg Glu 800 805 810	2572
	ctt gga ttt gct aaa atg ttg aga aag gac ctg Leu Gly Phe Ala Lys Met Leu Arg Lys Asp Leu 820 825	2620
	ttc agg ctt tca gcc cca gtt aga gac ctc ctg Phe Arg Leu Ser Ala Pro Val Arg Asp Leu Leu 835 840	2668
3 3 3	aaa cag tat gtc aag gtg caa att cct ggg tta Lys Gln Tyr Val Lys Val Gln Ile Pro Gly Leu 850 855	2716
	ttt gtt cca gac act ctt gct gag gag aag agt Phe Val Pro Asp Thr Leu Ala Glu Glu Lys Ser 865 870	2764
	ctc aat gca gct gca gga aag gac tgt tca aaa Leu Asn Ala Ala Ala Gly Lys Asp Cys Ser Lys 880 885 890	2812
	ctc atc gat gcc tat ctg ctt ctg acc aag cac Leu Ile Asp Ala Tyr Leu Leu Leu Thr Lys His	2860

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RTS-0169		-18-		PATENT
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ggt gat cga gcc	cgt gat tca ga	ag gac agc tgg ggd	acc tgg gag gca	2908
Gly Asp Arg Ala	Arg Asp Ser Gl	lu Asp Ser Trp Gly	Thr Trp Glu Ala	
910		915	920	
cag cct gtc aaa	gtc gtg cct ca	ag gtg gag act gtt	gac acc ctg aga	2956
Gln Pro Val Lys	Val Val Pro G	ln Val Glu Thr Val	Asp Thr Leu Arg	
925	93	30	935	
agc atg cag gtg	gat aat ctt tt	a cta gtt gtc ato	g cag tct gcg cat	3004
Ser Met Gln Val	Asp Asn Leu Le	eu Leu Val Val Met	Gln Ser Ala His	
940	945	950)	
ctc aca att cag	aga aaa gct tt	c cag cag tcc att	gag gga ctt atg	3052
Leu Thr Ile Gln	Arg Lys Ala Ph	ne Gln Gln Ser Ile	e Glu Gly Leu Met	
955	960	965	970	
act ctg tgc cag	gag cag aca to	cc agt cag ccg gto	atc gcc aaa gct	3100
Thr Leu Cys Gln	Glu Gln Thr Se	er Ser Gln Pro Val	l Ile Ala Lys Ala	
	975	980	985	
ttg cag cag ctg	aag aat gat go	ca ttg gag cta tgo	aac agg ata agc	3148
Leu Gln Gln Leu	Lys Asn Asp Al	la Leu Glu Leu Cys	s Asn Arg Ile Ser	
990		995	1000	
aat gcc att gac	cgc gtg gac ca	ac atg ttc aca tca	a gaa ttt gat gct	3196
Asn Ala Ile Asp	Arg Val Asp Hi	is Met Phe Thr Se	Glu Phe Asp Ala	
1005	10	010	1015	
gag gtt gat gaa	tct gaa tct gt	to acc ttg caa cag	g tac tac cga gaa	3244
Glu Val Asp Glu	Ser Glu Ser Va	al Thr Leu Gln Glr	n Tyr Tyr Arg Glu	
1020	1025	103	3 0	
gca atg att cag	ggg tac aat t	tt gga ttt gag tat	cat aaa gaa gtt	3292
Ala Met Ile Gln	Gly Tyr Asn Pl	he Gly Phe Glu Tyi	r His Lys Glu Val	
1035	1040	1045	1050)
gtt cgt ttg atg	tct ggg gag t	tt aga cag aag ata	a gga gac aaa tat	3340
Val Arg Leu Met	Ser Gly Glu Ph	he Arg Gln Lys Ile	e Gly Asp Lys Tyr	
	1055	1060	1065	
ata agc ttt gcc	cgg aag tgg at	tg aat tat gtc cto	g act aaa tgt gag	3388
Ile Ser Phe Ala	Arg Lys Trp Me	et Asn Tyr Val Lei	ı Thr Lys Cys Glu	

RTS-0169 -19-PATENT agt ggt aga ggt aca aga ccc agg tgg gcg act caa gga ttt gat ttt Ser Gly Arg Gly Thr Arg Pro Arg Trp Ala Thr Gln Gly Phe Asp Phe cta caa gca att gaa cct gcc ttt att tca gct tta cca gaa gat gac Leu Gln Ala Ile Glu Pro Ala Phe Ile Ser Ala Leu Pro Glu Asp Asp ttc ttg agt tta caa gcc ttg atg aat gaa tgc att ggc cat gtc ata Phe Leu Ser Leu Gln Ala Leu Met Asn Glu Cys Ile Gly His Val Ile gga aaa cca cac agt cct gtt aca ggt ttg tac ctt gcc att cat cgg Gly Lys Pro His Ser Pro Val Thr Gly Leu Tyr Leu Ala Ile His Arg aac agc ccc cgt cct atg aag gta cct cga tgc cat agt gac cct cct Asn Ser Pro Arg Pro Met Lys Val Pro Arg Cys His Ser Asp Pro Pro aac cca cac ctc att atc ccc act cca gag gga ttc agc act cgg agc Asn Pro His Leu Ile Ile Pro Thr Pro Glu Gly Phe Ser Thr Arg Ser atg cet tee gae geg egg age eat gge age eet get get get get get Met Pro Ser Asp Ala Arg Ser His Gly Ser Pro Ala Ala Ala Ala Ala get get get get get get gec agt egg eec age eec tet ggt ggt gac Ala Ala Ala Val Ala Ala Ser Arg Pro Ser Pro Ser Gly Gly Asp tot gtg ctg ccc aaa tcc atc agc agt gcc cat gat acc agg ggt tcc Ser Val Leu Pro Lys Ser Ile Ser Ser Ala His Asp Thr Arg Gly Ser age gtt cct gaa aat gat cga ttg gct tcc ata gct gct gaa ttg cag Ser Val Pro Glu Asn Asp Arg Leu Ala Ser Ile Ala Ala Glu Leu Gln ttt agg tcc ctg agt cgt cac tca agc ccc acg gag gag cga gat gaa Phe Arg Ser Leu Ser Arg His Ser Ser Pro Thr Glu Glu Arg Asp Glu

RTS-0169 -20-PATENT cca gca tat cca aga gga gat tca agt ggg tcc aca aga aga agt tgg Pro Ala Tyr Pro Arq Gly Asp Ser Ser Gly Ser Thr Arq Arq Ser Trp gaa ctt cgg aca cta atc agc cag agt aaa gat act gct tct aaa cta Glu Leu Arg Thr Leu Ile Ser Gln Ser Lys Asp Thr Ala Ser Lys Leu gga ccc ata gaa gct atc cag aag tca gtc cga ttg ttt gaa gaa aag Gly Pro Ile Glu Ala Ile Gln Lys Ser Val Arg Leu Phe Glu Glu Lys agg tac cga gaa atg agg aga aag aat atc att ggt caa gtt tgt gat Arg Tyr Arg Glu Met Arg Arg Lys Asn Ile Ile Gly Gln Val Cys Asp acg cct aag tcc tat gat aat gtt atg cac gtt ggc ttg agg aag gtg Thr Pro Lys Ser Tyr Asp Asn Val Met His Val Gly Leu Arg Lys Val acc ttc aaa tgg caa aga gga aac aaa att gga gaa ggc cag tat ggg Thr Phe Lys Trp Gln Arg Gly Asn Lys Ile Gly Glu Gly Gln Tyr Gly aag gtg tac acc tgc atc agc gtc gac acc ggg gag ctg atg gcc atg Lys Val Tyr Thr Cys Ile Ser Val Asp Thr Gly Glu Leu Met Ala Met aaa gag att cga ttt caa cct aat gac cat aag act atc aag gaa act Lys Glu Ile Arg Phe Gln Pro Asn Asp His Lys Thr Ile Lys Glu Thr gca gac gaa ttg aaa ata ttc gaa ggc atc aaa cac ccc aat ctg gtt Ala Asp Glu Leu Lys Ile Phe Glu Gly Ile Lys His Pro Asn Leu Val cgg tat ttt ggt gtg gag ctc cat aga gaa gaa atg tac atc ttc atg Arg Tyr Phe Gly Val Glu Leu His Arg Glu Glu Met Tyr Ile Phe Met gag tac tgc gat gag ggg act tta gaa gag gtg tca agg ctg gga ctt Glu Tyr Cys Asp Glu Gly Thr Leu Glu Glu Val Ser Arg Leu Gly Leu

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cag gaa cat gtg att agg ctg tat tca aag cag atc acc att gcg atc Gln Glu His Val Ile Arg Leu Tyr Ser Lys Gln Ile Thr Ile Ala Ile aac gtc ctc cat gag cat ggc ata gtc cac cgt gac att aaa ggt gcc Asn Val Leu His Glu His Gly Ile Val His Arg Asp Ile Lys Gly Ala aat atc ttc ctt acc tca tct gga tta atc aaa ctg gga gat ttt gga Asn Ile Phe Leu Thr Ser Ser Gly Leu Ile Lys Leu Gly Asp Phe Gly tgt tca gta aag ctc aaa aac aat gcc cag acc atg cct ggt gaa gtg Cys Ser Val Lys Leu Lys Asn Asn Ala Gln Thr Met Pro Gly Glu Val aac agc acc ctg ggg aca gca gca tac atg gca cct gaa gtc atc act Asn Ser Thr Leu Gly Thr Ala Ala Tyr Met Ala Pro Glu Val Ile Thr egt gee aaa gga gag gge eat ggg egt geg gee gae ate tgg agt etg Arg Ala Lys Gly Glu Gly His Gly Arg Ala Ala Asp Ile Trp Ser Leu ggg tgt gtt gtc ata gag atg gtg act ggc aag agg cct tgg cat gag Gly Cys Val Val Ile Glu Met Val Thr Gly Lys Arg Pro Trp His Glu tat gag cac aac ttt caa att atg tat aaa gtg ggg atg gga cat aag Tyr Glu His Asn Phe Gln Ile Met Tyr Lys Val Gly Met Gly His Lys cca cca atc cct gaa aga tta agc cct gaa gga aag gac ttc ctt tct Pro Pro Ile Pro Glu Arg Leu Ser Pro Glu Gly Lys Asp Phe Leu Ser cac tgc ctt gag agt gac cca aag atg aga tgg acc gcc agc cag ctc His Cys Leu Glu Ser Asp Pro Lys Met Arg Trp Thr Ala Ser Gln Leu ctc gac cat tcg ttt gtc aag gtt tgc aca gat gaa gaa tga agcctagtag 4976 Leu Asp His Ser Phe Val Lys Val Cys Thr Asp Glu Glu

-21-

gctggaaccc ctgaatccct

RTS-0169			-22-		F	'ATEN
1595	16	500	1609	5		
aatatggact	tggaaaattc	tcttaatcac	tactgtatgt	aatatttaca	taaagactgt	5036
gctgagaagc	agtataagcc	ttttaacct	tccaagactg	aagactgcac	aggtgacaag	5096
cgtcacttct	cctgctgctc	ctgtttgtct	gatgtggcaa	aaggccctct	ggagggctgg	5156
tggccacgag	gttaaagaag	ctgcatgtta	agtgccatta	ctactgtaca	cggaccatcg	5216
cctctgtctc	ctccgtgtct	cgcgcgactg	agaaccgtga	catcagcgta	gtgttttgac	5276
ctttctaggt	tcaaaagaag	ttgtagtgtt	atcaggcgtc	ccataccttg	tttttaatct	5336
cctgtttgtt	gagtgcactg	actgtgaaac	ctttaccttt	tttgttgttg	ttggcaagct	5396
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RTS-0169	-28-	PATENT
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